

**REMARKS**

Reconsideration is requested.

The specification has been amended to be consistent with the related, recently-issued application Serial No. 09/878,281, now U.S. Patent No. 6,762,024, which was examined by the examiner of the present application. The amendments to the specification of the related application to include sequence identifiers were require in an Office Action dated April 25, 2003. These amendments were not earlier made in the present application as it was only in reviewing the related application in preparation of this Amendment that the undersigned became aware of the fact that corresponding amendments had not yet been made in this related application. The amendments to the specification are not believed to introduce new matter or raise new issues requiring further search and/or consideration.

As explained in an Amendment dated August 25, 2003, in the related application Serial No. 09/878,281, the specification has been amended to include the heading "Brief Description of the Drawings" as suggested by the Examiner on page 2 of the Office Action dated April 25, 2003 (Paper No. 14) in the related application.

The applicants note that the undersigned's filing coversheet dated August 15, 2000, requested an amendment of the specification on page 1, to include a cross-reference to the parent application. The Examiner is requested to confirm that this amendment is entered in the application or advise the undersigned in the event anything further is required in this regard.

The specification has been amended to include the attached Sequence Listing as well as sequence identifiers corresponding therewith. The Patent Office is requested to

use the computer readable copy of the Sequence Listing filed August 25, 2003 in the related application Serial No. 09/878,281 for the present application. A separate Request for the same is attached herewith. The attached paper copy of the Sequence Listing is the same as the paper and computer readable copies of the Sequence Listing filed in the related application Serial No. 09/878,281 on August 25, 2003. No new matter has been added.

Page 33 has been amended above to correct an inadvertent typographical error. Support for the amendment may be found in, for example, Figure 5.

The applicants further note that page 39 has been amended as shown above to be consistent with amendments made in the related application Serial No. 09/638,693, and specifically, the applicants note that SEQ ID NOs:166, 168 etc., are mentioned on page 39 (penultimate and last bulleted point) of the description. SEQ ID NO:168 for instance has the sequence TCGF.....HRMA, as described in the Sequence Listing. Figure 5 indicates that the first amino acid T (thr) corresponds to amino acid 127 of the HCV polyprotein. Likewise, the last amino acid A (ala) of SEQ ID NO:168 corresponds to amino acid 319 of the HCV polyprotein (see Figure 5). The HCV Core protein spans positions 1-191 of the HCV polyprotein, the HCV E1 protein spans positions 192-383 of the HCV polyprotein. As SEQ ID NO:168 (and all other sequences of claim 87) starts at position 127, it will be understood to contain part of the Core protein. Hence, these sequences are to be regarded as Core/E1 proteins, as amended above. SEQ ID NO:166 is one of the sequences aligned in Figure 5 and spans amino acids 1-126 of the HCV polyprotein (MSTN.....IDTL) in accordance with SEQ ID NO:166 in Sequence Listing. As the HCV Core protein spans positions 1-191 of the

HCV polyprotein, SEQ ID NO:166 will be recognized by one of ordinary skill in the art as a Core protein, as amended above.

Page 40 (1st bulleted point) of the description has been amended above with regard to SEQ ID NO:192, which the Examiner will appreciate has the sequence MSTN.....WAGW, as described in the Sequence Listing. As will be clear from the description above with regard to SEQ ID NO:166, "MSTN...." refers to the start of the HCV polyprotein Core. SEQ ID NO:192 can be allocated amino acids 1-96 of the HCV Core polyprotein based on the sequence alignments in Figure 5. SEQ ID NO:192 is moreover one of the sequences aligned in Figure 5.

The specification has been further amended above on page 40 with regard to SEQ ID NOs:198 and 200. SEQ ID NOs:198 and 200 both cover the sequence CARTITT.....W(X/A)TY, as described in the Sequence Listing. SEQ ID NO:270 covers the sequence TITT.....WATY. SEQ ID NO:270 is one of the sequences aligned in Figure 7 (except for the first amino acid "T") and from Figure 7 one of ordinary skill in the art will appreciate that SEQ ID NO:270 spans amino acids 1284-1764 of the HCV polyprotein. SEQ ID NOs:198 and 200 both have 3 extra amino acids at their amino-terminus and thus span amino acids 1281-1764 of the HCV polyprotein. The common amino acids for the three SEQ ID NOs are 1284-1764.

No new matter has been added.

Claims 1-55, 57, 58, 60-74 and 86-91 have been canceled, without prejudice, above to advance prosecution. Upon entry of the above amendments, claims 56, 59 and 75-85 will be pending. Claim 75 has been indicated above as having been withdrawn however upon entry of the above amendments, the applicants believe claim

75 will be directed to elected subject matter such that upon entry of the above amendments, the applicants request examination of claim 75 along with claims 56, 59 and 76-85.

The claims, as amended above, are submitted to read on the elected subject matter.

Return of an initialed copy of the PTO-1449 Form filed May 8, 2001, is requested. The Patent Office PAIR system confirms that the Information Disclosure Statement and PTO-1449 Form filed May 8, 2001, have been received by the Patent Office and entered in the electronic file wrapper. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Reconsideration and withdrawal of the Section 112, second paragraph, rejection of claims 56, 59, 74 and 76-85 are requested as the amended claims are directed to the elected subject matter, do not specifically recite the objected to "genotype-specific amino acid", and have been amended to recite "optionally" in place of "possibly", as suggested by the Examiner on page 3, subparagraph (d) of the Office Action dated June 3, 2004.

The Examiner's continued assertion with regard to claim 74, as repeated in subparagraph (c) on page 3 of the Office Action of June 3, 2004, which refers to the comments of the Office Action of September 11, 2003, at page 3, item (c), is again not understood and clarification is requested. The Examiner is requested to appreciate that the "values" recite in claim 74, which have been canceled and are now recited in claim 56, refer to amino acid positions of the HCV polyprotein. The Examiner appears to believe the previously recitations of claim 74, and now claims 56 and 59, refer to ranges

or lengths of sequences however one of ordinary skill in the art will appreciate that the amino acid numberings of positions in claims 56 and 59, and in canceled claim 74, refer, for example, to the positions as exemplified in the figures, such as Figures 7 and 11, which provide sequence alignments of previously known HCV amino acid sequences and other HCV amino acid sequences. The Examiner is further requested to note that, in contrast to the numbering of nucleotides in the HCV genome, there is only a single numbering system for amino acid of the HCV polyprotein, namely starting with methionine at position 1 ("M1" in terms previously recited in claim 74 and now recited in claims 56 and 59), of the polyprotein. The applicants note that the relative numbering of the amino acids, may, however, vary among isolates/genotypes. See, the explanation in the third and fourth paragraphs on page 6 of the application as well as Table 1 of the page 27. The following listing and numbering of amino acids of SEQ ID NO:36 is provided for the Examiner's convenience and consideration.

Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala  
 1632 5 1641 15

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu  
 1651 1656 1661 1663

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys  
 35 1671 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val  
 1681 1685 55 1687 1689 1691 1695

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys  
 65 1701 75 1711

SEQ ID NO:99  
 Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln  
 1714 85 1721 1723 1726

SEQ ID NO:100  
 Phe Lys Gly Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln  
 1731 105 1741 1743

Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala  
 1744 115 1747 1749 1751 125 1759

Phe Trp His Lys His  
 1761 1762

SEQ ID NO:36 of Sequence Listing

Key:

Italicized numbers = numbering according to Sequence Listing  
 Bold numbers = position numbers according to HCV polyprotein  
 Bold underlined numbers = positions recited in claims 56 and 59  
 Bold underlined amino acids (aa) = aa recited in claims 56 and 59

Bracketed regions highlight regions of sequences of amended claim 75 as compared with the numbering of amino acids of SEQ ID NO:36

A review of the above will confirm for the Examiner that SEQ ID NO:36 is 133 residues and the "values" recited in claims 56 and 59, for example, relate to amino acid positions of the HCV polyprotein, as opposed to amino acid positions of SEQ ID NO:36. The recitation of claims 56 and 59 are submitted to be definite and will be, in the applicant's view, more readily recognizable to one of ordinary skill in the art as opposed to recitations of amino acid numbers which may reference SEQ ID NO:36.

The applicants submit, for the Examiner's convenience, that the amino acid numbers 1656, 1663, 1685, 1687, 1689, 1705, 1714, 1721, 1723, 1726, 1743, 1744, 1747, 1749, 1759 and 1762, of claims 56 and 59 correspond with amino acid positions 25, 32, 54, 56, 58, 74, 83, 90, 92, 95, 112, 113, 116, 118, 128 and 131, respectively of SEQ ID NO:36. This is clearly shown in the above depiction of SEQ ID NO:36 of the Sequence Listing. The applicants will be happy to amend claims 56 and 59 to refer to amino acid positions of SEQ ID NO:36 however the amended claims are submitted to be clear in their reference to and recitation of the numbering system used in the recitations of the claims. Claims 56, 59, 74 and 76-85, along with claim 75, are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection of the same are requested.

The Section 102 rejection of claims 56, 59, 74 and 76-85 over Simmonds (WO 93/10239), is traversed. Reconsideration and withdrawal of the rejection are requested as the applicants again submit that the claimed invention of the rejection should be accorded benefit of the priority document EP 93 401 099.2, which was filed April 27, 1993, i.e., prior to the May 27, 1993, date indicated by the Examiner as being the relevant date of the cited Simmonds reference. Specifically, the Examiner is requested

to see the following portions of the priority document EP 93 401 099.2 for disclosures of the claimed invention:

- "positions 1646 to 1764 in the NS3/NS4 region" and, in the same paragraph, "SEQ ID NO:36" (2<sup>nd</sup> bulleted point on page 19 of the priority document)
- the amino acid sequence of SEQ ID NO:36 is incorporated in the sequence listing (pages 76-77)
- SEQ ID NOs: 97, 99 and 100 are listed at the bottom of page 19 and are also incorporated in the sequence listing (pages 114-115)
- the last paragraph on page 15 of the priority document mentions as new type 3 amino acid sequences those deduced from the nucleotide sequences in SEQ ID NO 1 to 42. In particular, SEQ ID NO:36 is the deduced from the nucleotide sequence SEQ ID NO:35 (sequence listing, page 76 of the priority document) type 3-specific amino acids in the NS3/NS4 region are recited in the 1<sup>st</sup> list of amino acids in the middle of page 17 of the priority document .

A copy of relevant pages of the priority document are attached for the convenience and consideration of the Examiner.

Benefit of the priority document should be accorded the presently claimed invention and withdrawal of the Section 102 rejection of claims 56, 59, 74 and 76-85 over Simmonds is requested.

The Section 102 rejection of claims 56, 59, 74 and 76-85 over Chien (U.S. Patent No. 6,416,946), is similarly traversed. Withdrawal of the rejection is requested as the earliest date which appears to be applicable to the Chien reference is subsequent to the



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filing of the applicants' initial priority document. Moreover, the Examiner's indicated positions 26-31, 33-45 and 47-53 do not appear to be relevant to the presently claimed invention. Reconsideration and withdrawal of the Section 102 rejection of claims 56, 59, 74 and 76-85 over Chien are requested.

The claims are submitted to be patentable and in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



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